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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application	:	Stephen Fulghum
Application No.	:	10/092,033
Filed	:	March 5, 2002
Confirmation No.	:	7761
For	:	AUTOFLUORESCENCE IMAGING SYSTEM FOR ENDOSCOPY
Examiner	:	John P. Leubecker
Attorney's Docket	:	NLI-002AX

TC Art Unit: 3739

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Charles W. von Rosenberg, Jr., a resident of 247 Slade Street, Belmont, Massachusetts, hereby declare as follows:

1. My educational background includes a Bachelors Degree in Aeronautics & Astronautics from the University of Oklahoma in 1963, a Masters Degree in Aerospace Engineering from the Massachusetts Institute of Technology in 1965, a Ph.D. in Engineering Science from the University of Oklahoma in 1968, and post-doctorate research in Spectroscopy and Kinetics at the University of Southampton, England, in 1969.

2. I am the President and Chief Executive Officer of Newton Laboratories, Inc. of Belmont, Massachusetts, a position I have held since 1993. My duties in this position

include management and oversight of day-to-day operations and participation in research and development and technical review. Programs I have been involved with at Newton Laboratories include the development of diagnostic spectrofluorometers for detection of pre-cancerous conditions of the colon and lung by use of in vivo spectroscopy. Newton Laboratories, Inc. is the assignee of the above-captioned patent application, U.S. Application Ser. No. 10/092,033.

3. I have also served as Visiting Scientist at the MIT George R. Harrison Spectroscopy Laboratory since 1993, where I have consulted on research activities in the areas of laser ablation, laser induced fluorescence, scattering and other methods of tissue characterization using spectroscopy. I have also been a Principal Research Scientist/Engineer and Manager for Textron Systems Corporation (formerly Avco Everett Research Laboratory), with research in the area of lasers and electro-optics. I have served on the patent committee at Textron.

4. I am familiar with U.S. Patent Application Ser. No. 10/092,033, and I have read the application and examined the drawings for the application. I understand that this application is a continuation of U.S. Patent Application Ser. No. 09/362,806 filed on July 28, 1999, which is a continuation-in-part of U.S. Patent Application Ser. No. 09/238,664 filed on January 26, 1999.

5. I have read the pending claims of the present application, and the Final Office Action dated November 20, 2008 in the present application.

6. One of ordinary skill in the art of fluorescence-based diagnostic systems, reading the present application as filed, would understand that the applicants were clearly in

possession of a fluorescence imaging endoscope system having a diode laser source for producing excitation light.

7. One skilled in the art would understand from the Summary of the Invention, specifically at page 5, lines 4-6, that in a preferred embodiment, light in the range of 300-420 nm is chosen as the excitation wavelength. The specification further describes at page 8, lines 23-28 that in some embodiments, the excitation illumination and the reference illumination are generated by the same arc lamp source, and in other embodiments, the excitation light can be generated with a stand-alone source. This is further confirmed in Figures 11a-11d and 12, and in the related discussion at pages 25-27 of the specification, which describe and illustrate embodiments having a separate stand-alone excitation light source, and more particularly a UV or UV/Violet excitation light source (see, e.g., reference number 1128 in Fig. 11b; and "UV/VIOLET SOURCE IMAGE" in Fig. 12).

8. From page 10, lines 13-20, one skilled in the art would understand that a number of different excitation light sources, including argon-ion lasers, solid state lasers, such as gallium nitride laser diodes operating at wavelengths in the range of 380 nm to 420 nm, and a mercury arc lamp with a spectral band around the 365 nm mercury line, were all contemplated by the inventors as part of their invention.

9. I disagree with the contention in the Final Office Action that the disclosure of the present invention is specifically directed to the use of an arc lamp as the excitation source. The statement on page 10, lines 16-18 of the specification that "[t]he systems in accordance with the present invention uses [*sic*] a mercury arc lamp as a source of UV excitation with a spectral band around the 365 nm mercury line" would not be

understood by one of ordinary skill as limiting the invention to only the described mercury arc lamp source, to the exclusion of all other sources. One reason for this is that the Summary of the Invention does not mention any particular excitation sources, but instead states that light in the range of 300-420 nm can be chosen as the excitation wavelength in a preferred embodiment of the invention. (See page 5, lines 4-6). Thus, one skilled in the art would understand that the mercury arc lamp with a spectral band around the 365 nm mercury line is one example of a suitable excitation source, but that other sources operating at other wavelengths within the described range could also be used.

10. Further, one skilled in the art would read the passage at page 10, lines 13-20 as describing three examples of excitation sources suitable for the described fluorescence imaging endoscope system, namely an argon-ion laser as described in the Wang, *et al.* document, a solid state laser operating in the 380 nm to 420 nm wavelength range, and a mercury arc lamp with a spectral band around the 365 nm mercury line. The statement that "[o]ther laser sources can be used including solid state lasers, such as gallium nitride laser diodes, operating at wavelengths in the range of 380 nm to 420 nm," is a clear indication to one skilled in the art that diode laser light sources are encompassed within the fluorescence imaging endoscope system of the invention.

11. The statement of comparison between the argon-ion laser and the mercury arc lamp (p. 10, lines 18-20: "The mercury arc lamp is smaller, and less expensive than the argon-ion laser, requires relatively little power and is air-cooled") is irrelevant to the question of whether one skilled in the art would consider a diode laser light source as being part of the subject invention. The comparison made in that passage is between an argon-ion laser and a mercury arc lamp, and does not involve a diode laser source.

Furthermore, the application also favorably compares diode laser sources to the argon-ion laser, noting their "smaller size and low power operation" (page 10, line 16), which further indicates that diode laser sources were contemplated as part of the invention.

12. I disagree with the statements in the Office Action that the diode laser is mentioned with respect to "prior knowledge," and that the specification would imply to the reasonable person that diode lasers "have been considered in the art but are not for use in the present invention." To my knowledge, diode laser sources had not been known or described in the art for use as an excitation source in an autofluorescence imaging endoscope system as of July 28, 1999, which I understand to be the effective filing date of the present application. Therefore, the fact that the specification states that diode lasers can be used, when they had not previously been known for this use, and further describes their advantages relative to the previously-known argon-ion laser source, clearly indicates to the ordinarily skilled artisan that a diode laser excitation source was encompassed by the subject invention.

13. I disagree with the statements in the Office Action that the description at page 12, lines 2-4 of the specification would be understood as supporting only the use of a mercury arc lamp and not the use of a diode laser operating at a wavelength in the range of 380 to 420 nm. Although it may the case that an excitation source operating in certain portions of this wavelength range might overlap with the sensitivity range of certain types of detectors, the specification would not be understood as excluding the use of wavelengths within the 380 to 420 nm range. One skilled in the art would understand that where the excitation wavelength overlaps with the detector sensitivity range, the detector can be made insensitive to the excitation wavelength through the use of one or more filters. In fact, this is explicitly taught in the present specification at

page 7, lines 24-26, which states that "[t]he use of a camera at the distal end is made possible by using fluorescence excitation light at ultraviolet to deep violet wavelengths to which the CCD camera is insensitive *or can be made insensitive using a fixed filter*" (emphasis added). This is further supported in the Summary of the Invention, which teaches that excitation wavelength in the range of 300-420 nm "reduces or eliminates" the need for filters between the tissue and the imaging detector due to the fact that standard, electronic image sensors are insensitive to the excitation light. (See page 5, lines 6-9). Thus, the present invention clearly contemplates embodiments in which there is some overlap between the excitation wavelength and the detector sensitivity range, which can be addressed, for instance, by the use of filters. This is further supported by the Wang *et al.* disclosure, Application No. 09/238,664, now U.S. Patent 6,537,211, which is incorporated by reference in the present application. As noted by the Examiner, Wang *et al.* note that the spectral response of a CCD detector falls off to zero below 400 nm, and therefore the CCD detector can serve as its own long-pass filter. However, Wang *et al.* further teach that "other imaging devices can be used with a filter" to reduce the detected intensity in the ultraviolet (excitation) region relative to the detected intensity in the visible region. (See U.S. Patent 6,537,211 at col. 2, lines 9-17). The Wang *et al.* patent specifically describes the use of a detector with a long-pass filter at col. 18, lines 38-41.

14. One of ordinary skill in the art of fluorescence-based diagnostic systems, reading the present application as filed, would understand that the applicants were clearly in possession of the subject matter of claim 7, namely a control system that emits control signals such that excitation light and the reference light are emitted simultaneously such the respective images are detected by a color-sensitive image detector, a blue channel

detecting the fluorescence image and a red channel detecting the reference image, for example.

15. One of ordinary skill in the art would understand from, for example, page 8, line 28 through page 9, line 3 of the specification, that the reference light illumination can be derived from the normal white light illumination source by switching in a red-pass filter that absorbs light at blue and green wavelengths in one embodiment. This is shown, for example, in the embodiment of Figs. 11a-11d, and described at page 26, lines 13-23 of the specification. More specifically, as shown and described in this embodiment, a first light source 1128 provides excitation light, and a second light source 1118 produces a reference light. Because the reference light source 1118 is the normal white light illumination source, it inherently includes red, green and blue wavelength bands. A filter 1132 is operable to selectively switch between white light illumination and one example of reference light illumination by strongly attenuating UV, blue and green wavelengths from the second light source 1118. Furthermore, the specification specifically states that in certain embodiments, the tissue is illuminated by both the UV excitation light and the reference light simultaneously. (page 26, lines 18-19). The specification describes at, for example, page 24, lines 10-25, that the respective images can be detected by a color-sensitive image detector, namely a color-sensitive CCD detector, with a blue channel (blue-responsive pixels) detecting the fluorescence image, and a red channel (red-responsive pixels) detecting the reference image. It is further desirable to detect a color image having red green and blue components in combination with a fluorescence image using either a color sensitive imaging detector or by detecting these three colors separately using a monochromatic imaging detector.

16. I declare further that all statements made herein to my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dec 22, 2009
Date

Charles W. von Rosenberg, Jr.

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